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Preface

Alzheimer's disease (AD) is widely known by the general public to be the most common cause of cognitive decline in the elderly. As one of the most conspicuously malfunctioning proteins in AD, tau has likewise become recognized by physicians and biomedical researchers as a potential target of therapeutic intervention, and at the very least, as a gene product whose fundamental roles in the cell demand much further exploration. The early history of tau did not predict its current notoriety. When its discovery was announced nearly three decades ago [1], tau primarily attracted the interest of a small group of laboratories working on in vitro microtubule assembly and how it might relate to microtubule dynamics in the mitotic spindle. When it became clear 10 years later that tau is primarily expressed in neuronal cell axons [2], interest in tau waned among mitosis aficionados, although the protein did capture the attention of neuroscientists as an axon marker for immunohistochemistry.

Attention to tau rose dramatically soon thereafter following reports that it is abnormally phosphorylated in AD [3] and is the building block of neurofibrillary tangles, one of the histopathological hallmarks of AD [4,5]. Ensuing reports that AD can be caused by mutations in the genes for β-amyloid precursor protein [6] and presenilins [7,8] lessened interest in tau since no genetic link between tau and AD was forthcoming.

Beginning in late 1998, a steady and still uninterrrupted stream of evidence has demonstrated tight linkage between tau mutations and frontotemporal dementias. These diseases share many fundamental features of AD: neurodegeneration, loss of cognitive function, accumulation of filamentous tau aggregates comprising hyperphosphorylated tau, and ultimately the death of the afflicted individuals [9–12]. These findings constitute irrefutable evidence that impaired tau function, whether it is caused by a faulty tau gene or other factors that can affect tau, can lead directly to the debilitating phenotypes of all "tauopathies", including AD.

Tau is thus in the limelight again. The purpose of this Special Issue of *Biochimica et Biophysica Acta: Molecular Basis of Disease* is to provide the research community, for the first time ever, with a collection of articles that deals with cutting-edge research on tau and appears in a dedicated issue of a journal that is widely available in libraries and online throughout the world. We thank Biochimica et Biophysica Acta and its parent company, Elsevier Science, for agreeing to support our plan, and hope this Special Issue proves to be a valuable and timely resource to all those who are interested in the molecular basis of AD and non-AD tauopathies.

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